

REMARKS

The newly assigned Examiner in this application apparently believes that he can blithely ignore nine years of prosecution. The Examiner is wrong. Indeed, The Examiner's regurgitation of rejections which were overcome during the course of those nine years of prosecution, and the overturning of an agreement to allowance of specific claims in this application, are not supported by the Patent Office rules, the applicable statutes, the M.P.E.P., or common decency.

Applicants will, of course, demonstrate why the rejections made in this case are wrong. That is the easy part. The more difficult part is explaining how an Examiner can implicate himself into this case at this stage in the prosecution and totally ignore everything that has occurred in this case since 1997. Indeed, the Examiner has the audacity to rely on parts of the M.P.E.P. in this rejection. Applicants will demonstrate below that the portions of the M.P.E.P. relied upon by the Examiner are incorrectly and improperly utilized. The Examiner fails to note, however, rules such as M.P.E.P. § 706.04 requiring that great care be exercised in authorizing rejection of a claim which has been deemed allowable. This section of the M.P.E.P. then goes on to require that the Examiner give "full faith and credit" to the actions of previous Examiners. The Examiners are cautioned not to take "an entirely new approach or attempt to reorient the point of view of a previous Examiner. . . ." Indeed, the Examiner does not even apply Form Paragraph 7.50 as required by the M.P.E.P. in this case of a previous indication of allowability. However, even that section of the M.P.E.P. requires reliance on newly discovered references, which, of course, is not the case here. In this case, without even making the effort to justify his conduct, the Examiner does not even rely on any new references,

but instead merely resurrects references that were last applied many years ago.

The allegedly "new" non-final rejections which are, in fact, mere replays of various prior rejections in this case, include an allegation that claims 1 and 3-16 are unpatentable over Bardin et al. in view of Reed et al. under 35 U.S.C. § 103(a). This rejection is respectfully traversed for the reasons submitted during the course of the prosecution of this application and for the following additional reasons.

The Examiner begins by quoting from Bardin et al., in particular from claim 4 thereof, which, of course, is the only disclosure in that entire reference which refers to the word "transdermal" at all. This, of course, has been one of the issues which has been central to the prosecution of this application and which had apparently been overcome prior to the latest official action. In any event, however, the Examiner then contends that transdermal administration of from 5 to 10  $\mu\text{g}/\text{kg}$  of body weight of  $7\alpha$ -methyl-19-nortestosterone allegedly overlaps the range of that compound delivered by the presently claimed dosage form for a 70 kg male. This is the first error made by the Examiner. Claim 1 calls for an amount of the  $7\alpha$ -methyl-19-nortestosterone sufficient to deliver between about 400 to about 1600 micrograms in bioavailable form over a 24-hour period. Claim 4 of Bardin et al. merely states that the amount to be delivered transdermally is 5 to 10  $\mu\text{g}$  per kilogram, or 0.35 to 0.7 milligrams of testosterone derivative, clearly not a sufficient amount to deliver the claimed amount of this drug. As has been spelled out throughout the prosecution of this case, and as is set forth, for example, in the previously filed declaration of Dr. Radlmaier, from 5 to 10  $\mu\text{g}/\text{kg}$  of body weight is far too low to be useful for purposes of this invention, and clearly represents insufficient amounts

to be placed in a transdermal product for this particular drug. Dr. Radlmaier thus refers to a Phase One study that has determined that the total bioavailability of  $7\alpha$ -methyl-19-nortestosterone given transdermally is about 10%. Thus, effective treatment of hypogonadal males would require transdermal application of at least from 5 to 10 mg of this drug. The claims in this application require a sufficient amount to deliver between about 400 and about 1600 mg of this androgen in bioavailable form over a 24-hour period, and Bardin et al. fails to suggest or teach that this can or should be done, even in the single reference in claim 4 to any transdermal material. Indeed, Bardin et al. has a mere fortuitous reference to transdermal in claim 4 of the patent, but essentially teaches intravenous application of the drug, in which none of the problems of transdermal treatment, flux rate through the skin, and/or the need for specific dosage amounts as are set forth in the claims in this application, were even considered, much less discussed, in this reference. This much has been verified by the declaration of Bardin himself in this case.

Indeed, this is a particularly good example of why the M.P.E.P. requires Examiners to give full faith and credit to the actions of prior Examiners. When these issues first arose, and the prior Examiner made these same assertions, the Bardin et al. disclosure was considered in excruciating detail. The fact that Bardin et al. is really directed to intravenous or subcutaneous application of this drug throughout its entire specification made it clear that the single, fortuitous and unsupported reference to "transdermal" in claim 4 makes no sense. In the former case, there is obviously no problem providing the claimed amount of drug in bioavailable form — one simply injects it directly into the body. In the latter case, without any explanation whatsoever of how one is to provide any amount of bioavailable drug transdermally, there is no teaching of the

claimed invention. The prior Examiner understood this fact — that is why these claims are in allowable form. Starting over with the prosecution of this application at this point cannot be justified.

The Examiner then goes on to admit that Bardin et al. "does not teach the transdermal dosage form used in the method." Reed et al. is then relied upon. Firstly, the Reed et al. reference, whose publication date is about one month prior to the filing date of applicants' provisional application, relates in general to percutaneous or transdermal drug delivery systems. After recognizing the many difficulties in various transdermal applications, these patentees claim the use of penetration enhancers, particularly safe, skin-tolerant, ester sunscreens. After mentioning a number of dosage forms, including creams, lotions, gels, suppositories, mousses, sprays, aerosols, buccal and sublingual tablets, gingival and buccal patches, or a variety of transdermal devices, which fail to even mention transdermal patches (except for gingival and buccal patches, a specific category of same for use in the mouth), this patentee goes on to describe a broad range of vehicles for these compounds. Among the hundreds of drugs which are then listed (see pages 7-16 of Reed et al.), is listed 7 $\alpha$ -methyl-19-nortestosterone. No specific details are given with respect to the nature of these systems or the amount of drug employed, as compared, for example, to Bardin et al.

In any event, however, and in order to expedite the prosecution of this application, attached hereto is a Declaration under Rule 131 by Dr. Tsong, demonstrating that Reed et al. is not a reference against this application. The Declaration shows unequivocally that the applicants made the presently claimed invention and that in fact it was actually reduced to practice before the publication date of Reed et al. Therefore, Reed et al. is not a proper reference hereagainst,

and this entire rejection no longer has any basis in law or in fact.

The Examiner then goes on to refer to other sections of the M.P.E.P. The sections quoted by the Examiner refer to situations where the prior art products are substantially identical to the claimed products. The Examiner, for example, cites *In re Spada*, 911 F.2d 705, 709, 15 U.S.P.Q.2d 1655, 1658 (Fed. Cir. 1990) for the proposition that "[w]hen the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." The Examiner goes on to sight M.P.E.P. § 2112.01, paragraph II for the contention that products of identical chemical compositions cannot have mutually exclusive properties. Thus, it is stated that if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

The difficulty arises when one tries to determine how these citations apply to this case. Firstly, the Examiner is referring in this case to a combination of references which is being applied under § 103(a). This is not even an anticipation rejection, and does not amount to an assertion that the identical compound being claimed is in the prior art. The Examiner then goes on to admit that Bardin et al. and Reed et al. do not disclose the herein claimed preferred weight percentage of 7 $\alpha$ -methyl-19-nortestosterone in a transdermal delivery system! Admitting that the prior art does not teach the identical claimed chemical composition, all of the Examiner's reference to the M.P.E.P. and case law such as *In re Spada* becomes inapposite. Indeed, the very fact that the Examiner is relying upon a combination of references to allegedly obviate this invention in and of itself makes it clear that these principles have no application whatsoever to this case. The Examiner has admitted that the cited prior art does

not teach the same composition as that being claimed. This is an obviousness rejection, which has previously been overcome by extensive argument, and the presentation of affidavit evidence. Applicants have more than met any burden of proof which the Examiner can establish, and indeed the Examiner does not set forth a *prima facie* case for unpatentability at this point in the prosecution.

In then trashing the Bardin declaration submitted by the applicants, and merely making the broad statement that a non-enabling reference may qualify as prior art (not disputed), the Examiner falls back on an allegation that Bardin *et al.* provides sufficient motivation for one to look for references teaching known formulations for transdermal delivery of 7 $\alpha$ -methyl-19-nortestosterone in Bardin *et al.*'s method. Reference is then again made to Reed *et al.*, but at this point applicants have more than amply demonstrated that Reed *et al.* is not a proper reference hereagainst. Indeed, even if it were, Reed *et al.* includes 7 $\alpha$ -methyl-19-nortestosterone among hundreds of potential drug compounds, even in the context of that overall disclosure.

Applicants would request that the Examiner therefore review the entire history of this case, including the declarations of Messrs. Radlmaier and Bardin, and the previous declaration of Dr. Moo-Young, and the comparative data in the specification, as well as the extensive arguments previously presented as to the deficiencies of Bardin *et al.* and of the other references cited hereagainst. All of these arguments have been countered in the past, successfully in fact, and the Examiner has provided no basis for reversing the prior Examiner's position in this regard.

Claims 1, 3-6, and 13-16 have been rejected as being unpatentable over Jain *et al.* in view of Bardin *et al.* under

35 U.S.C. § 103(a). Applicants first discussed a rejection based on Jain et al. in response to an office action of July 9, 1999, in this case. Even at that time, applicants pointed out that references such as Jain et al. failed to identify even non-5 $\alpha$ -reducible androgens as were then being claimed, much less the 7 $\alpha$ -modified androgens such as 7 $\alpha$ -methyl-19-nortestosterone to which the claims are now directed. The mere recitation of broad genera of androgens was not only established as being non-anticipatory, but this patent was said to have a broad enough disclosure so that thousands of steroid-based compositions, including androgens, were set forth therein. Applicants thus pointed out that a generic recitation which reads on so many compounds cannot possibly "disclose" and therefore anticipate each and every species contained within its scope, citing *In re Rushig*, 379 F.2d 990 (C.C.P.A. 1967). Indeed, it was pointed out at the time that Jain et al. identifies as its preferred androgens testosterone and esters thereof (col.5, l.7). Testosterone, however, is 5 $\alpha$ -reducible, and therefore represents the antithesis of the present invention. Again in this regard, reference is made to the comparative data discussed in detail in both the specification and throughout the early stages of the prosecution of this application.

Subsequently, reference to Jain et al. was withdrawn, and it has not been since 2001, some five years ago, that this reference has been cited against these claims. Nevertheless, Jain et al. returns, and on the same basis that was previously the case! Indeed, in the combination of these references now relied upon by the Examiner, the Examiner attempts to combine these references without a clear and logical basis therefor. It is therefore respectfully requested that at least this rejection be withdrawn at this point, just as it was over five years ago.

Claim 23 has been rejected as being unpatentable over Bardin *et al.* in view of Reed *et al.*, and furthermore in view of Moo-Young *et al.* under 35 U.S.C. § 103(a).

Applicants have discussed in detail above the clear deficiencies of Bardin *et al.* and Reed *et al.* with respect to the present claims, as well as establishing that Reed *et al.* is not a proper reference in the first instance. Furthermore, reliance upon the Moo-Young *et al.* patent at this stage in the prosecution of this case is almost incomprehensible. Moo-Young *et al.* has been cited in the specification of this application from the outset. This reference has been before the Examiner for nine years, and now, for the first time, it is applied against the claims. Moo-Young *et al.* in any event is only cited for its teaching of an acetate salt of 7 $\alpha$ -methyl-19-nortestosterone. Therefore, since applicants do not pretend to have invented the acetate form of any drug, the additional citation of Moo-Young *et al.* provides nothing of value with respect to the basic limitations in these claims. Applicants therefore respectfully submit at this time that claim 23, like the other claims in this case, is clearly patentable over the art, and reconsideration of this rejection is also respectfully requested.

Claim 23 has also been rejected as being unpatentable over Jain *et al.* in view of Bardin *et al.*, and further in view of Moo-Young *et al.* under 35 U.S.C. § 103(a). Again, however, since each of these references has been discussed in detail, and all have been cited for years in the course of this application, and since this rejection is only directed to claim 23, based upon the allegation that Moo-Young *et al.* teaches the acetate salt of the claimed compound, it is submitted that detailed discussion of this rejection is not necessary at this time.

Claims 1, 3-6 and 23 have been rejected as being unpatentable on the basis of obviousness-type double patenting

over claims 1-11 and 14-23 in co-pending Application No. 10/741,407. However, in view of the fact that this is a provisional rejection, and since no patent has been allowed based on the cited application, detailed discussion of this rejection is unnecessary at this time.

In summation, while the Examiner might believe that the nine-year history of this application is irrelevant to consideration of the patentability of these claims, applicants, and the M.P.E.P. itself, tell us otherwise. Certainly no patent should issue unless it is patentable over the art. That issue, however, has been the subject of in-depth prosecution for nine years, and indeed the prior Examiner agreed to the allowable nature of claim 1 in this application prior to the latest official action herein. The mere fact, however, that a new Examiner has been assigned to this case, cannot become a substitute for this entire nine-year history, nor an open door for the citation of art which has been before the Patent Office and, in fact, cited by the Patent Office throughout that period. In view of the nature of this art, the overwhelming evidence of unexpected results, the admitted differences between the art and the cited references, the fact that one of the major references is not even applicable, and the utter failure of Bardin et al. to constitute a real teaching reference with respect to transdermal treatment with any drug, much less 7 $\alpha$ -methyl-19-nortestosterone, it is believed that this application should be considered to remain in condition for allowance at this time.

Finally, it is also respectfully requested that, upon consideration of this case, the Examiner telephone applicants' attorney at 908-654-5000 in order to discuss the status of the Examiner's consideration of this case, and/or the need or propriety of a further personal interview with the Examiner if that is believed to be helpful. Again, reconsideration and allowance of these claims is respectfully solicited.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

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Respectfully submitted,

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